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 NEWS  4  May 12   Polymer links for the POLYLINK command completed in REGISTRY
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 NEWS 11  AUG 02   IFIPAT/IFIUDB/IFICDB reloaded with new search and display
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=> s nuclear (s) hormone (s) receptor (s) homodimer
L1 185 NUCLEAR (S) HORMONE (S) RECEPTOR (S) HOMODIMER

=> s nuclear (s) hormone (s) receptor (s) homodimer (s) fusion
L2 4 NUCLEAR (S) HORMONE (S) RECEPTOR (S) HOMODIMER (S) FUSION

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 4 DUP REM L2 (0 DUPLICATES REMOVED)

=> d l3 total ibib kwic

L3 ANSWER 1 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2004003797 EMBASE
TITLE: Functional specificity of two hormone response elements present on the human apoA-II promoter that bind retinoid X receptor α/thyroid receptor β heterodimers for retinoids and thyroids: Synergistic interactions between thyroid receptor β and upstream stimulatory factor 2a.
AUTHOR: Hatzivassiliou E.; Koukos G.; Ribeiro A.; Zannis V.; Kardassis D.
CORPORATE SOURCE: D. Kardassis, Department of Basic Sciences, University of Crete Medical School, Inst. of Molec. Biol. and Biotech., Herakleion GR-71110, Greece. kardasis@imbb.forth.gr
SOURCE: Biochemical Journal, (1 Dec 2003) 376/2 (423-431).
Refs: 40
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . binding and mutagenesis in vitro established that the -67/-55 region of the apoA-II (apolipoprotein A-II) promoter contains a thyroid HRE (**hormone** response element), which strongly binds RXRα (retinoid X **receptor** α)/T(3)Rβ (thyroid **receptor** β) heterodimers and weakly T(3)Rβ **homodimers**, but does not bind other homo- or heterodimers of RXRα or orphan **nuclear receptors**. Transactivation was abolished by point mutations in the thyroid HRE. In co-transfection experiments of HEK-293 (human embryonic kidney 293) cells,. . . 2a) synergistically transactivated the -911/+29 apoA-II promoter in the presence of T(3). USF2a also enhanced the activity of a GAL4-T(3)Rβ **fusion** protein in the presence of T(3) and suppressed the activity of a GAL4-RXRα **fusion** protein in the presence of RA. These findings suggest a functional specificity of the two HREs of the apoA-II promoter. . .

L3 ANSWER 2 OF 4 MEDLINE on STN
ACCESSION NUMBER: 2003199690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12719467
TITLE: Active repression by unliganded retinoid receptors in development: less is sometimes more.
AUTHOR: Weston Andrea D; Blumberg Bruce; Underhill T Michael
CORPORATE SOURCE: Institute for Systems Biology, 1441 N. 34th St., Seattle, WA 98103, USA.. aweston@systemsbiology.org
SOURCE: Journal of cell biology, (2003 Apr 28) 161 (2) 223-8. Ref: 49
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030430
Last Updated on STN: 20030620
Entered Medline: 20030619
AB . . . APL, acute promyelocytic leukemia; dnRARalpha, dominant-negative version of the RARalpha; E, embryonic age; HDAC, histone deacetylase; LCoR, ligand-dependent corepressor; NCoR, **nuclear receptor** corepressor; RA, retinoic acid; RAR, RA **receptor** ; RARE, RXR **homodimer** bound to bipartite response element; RXR, retinoid X **receptor**; TSA, trichostatin A; CYP26, cytochrome p450, 26; TR, thyroid **hormone receptor**. **receptor** (RAR) **fusion** proteins, blocks myeloid differentiation leading to a rare form of leukemia. Our current understanding of the developmental role of retinoid. . .

L3 ANSWER 3 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998227564 EMBASE
TITLE: Interaction of BAG-1 with retinoic acid receptor and its inhibition of retinoic acid-induced apoptosis in cancer cells.
AUTHOR: Liu R.; Takayama S.; Zheng Y.; Froesch B.; Chen G.-Q.; Zhang X.; Reed J.C.; Zhang X.-K.
CORPORATE SOURCE: X.-K. Zhang, Burnham Institute, Cancer Research Center, 10901 N. Torrey Pines Rd., San Diego, CA 92037, United States. xzhang@ljcrf.edu
SOURCE: Journal of Biological Chemistry, (3 Jul 1998) 273/27 (16985-16992).
Refs: 52
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB BAG-1 (also known as HAP46) is an anti-apoptotic protein, which has been shown previously to interact with a number of **nuclear hormone receptors**, including **receptors** for glucocorticoid, estrogen, and thyroid **hormone**. We show here that BAG-1 also interacts with retinoic acid **receptor** (RAR). Gel retardation assays demonstrated that in vitro translated BAG-1 protein could effectively inhibit the binding of RAR but not retinoid X **receptor** (RXR) to a number of retinoic acid (RA) response elements (RAREs). A glutathione S- transferase-BAG-1 **fusion** protein also specifically bound RAR but not RXR. Interaction of BAG-1 and RAR could also be demonstrated by yeast two-hybrid assays. In transient transfection

assays, co-transfection of BAG-1 expression plasmid inhibited the transactivation activity of RAR/heterodimers but not RXR/RXR **homodimers**. When stably expressed in breast cancer cell lines, BAG-1 inhibited binding of RAR/RXR heterodimer to a number of RAREs and. . .

L3 ANSWER 4 OF 4 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2000303761 EMBASE
TITLE: Estrogen receptor, a common interaction partner for a subset of nuclear receptors.
AUTHOR: Lee S.-K.; Choi H.-S.; Song M.-R.; Lee M.-O.; Lee J.W.
CORPORATE SOURCE: Dr. J.W. Lee, College of Pharmacy, Hormone Research Center, Chonnam National University, Kwangju 500-757, Korea, Republic of. jlee@chonnam.chonnam.ac.kr
SOURCE: Molecular Endocrinology, (1998) 12/8 (1184-1192).
Refs: 59
ISSN: 0888-8809 CODEN: MOENEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Nuclear receptors** regulate transcription by binding to specific DNA response elements as **homodimers** or heterodimers. Herein, the yeast and mammalian two-hybrid tests as well as glutathione-S-transferase pull-down assays were exploited to demonstrate that estrogen **receptor** (ER) directly binds to a subset of **nuclear receptors** through protein-protein interactions between ligand-binding domains. These **receptors** include hepatocyte **nuclear** factor 4, thyroid **hormone** **receptor** (TR), retinoic acid **receptor** (RAR), ERβ, and retinoid X **receptor** (RXR). In yeast cells, a LexA **fusion** protein to the human ER ligand-binding domain (LexA/ER-LBD) was an inert transactivator of a LacZ reporter gene controlled by upstream. . . LexA/ER-LBD differentially modulated the LacZ reporter gene expression when coexpressed with native TRs, RARs, or RXRs. Similarly, cotransfection of these **receptors** in CV1 cells up- or down-regulated transactivations by ER. From these results, we propose that ER is a common interaction partner for a subset of **receptors**, and these interactions should mediate novel signaling pathways in vivo.

=> s nuclear (s) hormone (s) receptor (s) homodimer (s) chimera
L4 1 NUCLEAR (S) HORMONE (S) RECEPTOR (S) HOMODIMER (S) CHIMERA

=> d l4 ibib kwic

L4 ANSWER 1 OF 1 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96064834 EMBASE
DOCUMENT NUMBER: 1996064834
TITLE: Selective effects of ligands on vitamin D3 receptor- and retinoid X receptor-mediated gene activation in vivo.
AUTHOR: Lemon B.D.; Freedman L.P.
CORPORATE SOURCE: Cell Biology and Genetics Program, Memorial Sloan-Kettering Cancer Ctr., 1275 York Ave.,New York, NY 10021, United States
SOURCE: Molecular and Cellular Biology, (1996) 16/3 (1006-1016).
ISSN: 0270-7306 CODEN: MCEBD4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry

LANGUAGE: English
SUMMARY LANGUAGE: English
AB Steroid/**nuclear hormone receptors** are ligand-regulated transcription factors that play key roles in cell regulation, differentiation, and oncogenesis. Many **nuclear receptors**, including the human 1,25- dihydroxyvitamin D3 **receptor** (VDR), bind cooperatively to DNA either as **homodimers** or as heterodimers with the 9-cis retinoic acid (RA) **receptor** (retinoid X **receptor** [RXR]). We have previously reported that the ligands for VDR and RXR can differentially modulate the affinity of the **receptors'** interaction with DNA in vitro, primarily by modulating the dimerization status of these **receptors** . These experiments suggested a complex interaction between VDR and RXR and their respective ligands on inducible target genes in vivo.. . . we simultaneously introduced two different reporter plasmids that are selectively inducible by each ligand. Although VDR can bind as a **homodimer** to the osteopontin gene vitamin D response element, we find that a RXR-VDR heterodimer must be the transactivating species from. . . from an RXR-responsive element. These effects, however, appear to be very sensitive to both the relative ratios of the two **receptors** and their respective target elements. Functional RXR-VDR complexes are strictly dependent on their DNA-binding polarity. Chimeric versions of VDR and RXR were also constructed to examine the putative activities of homodimeric **receptors**; a VDR **chimera** can transactivate in the absence of RXR, demonstrating that VDR has intrinsic transactivation properties. Taken together, these results establish a complex, sensitive cross talk in vivo between two ligands and their **receptors** that signal through two distinct endocrine pathways.

=> s nuclear (s) receptor (s) homodimer (s) fusion
L5 16 NUCLEAR (S) RECEPTOR (S) HOMODIMER (S) FUSION

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 16 DUP REM L5 (0 DUPLICATES REMOVED)

=> d 16 total ibib kwic

L6 ANSWER 1 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004008126 EMBASE
TITLE: Probing protein oligomerization in living cells with fluorescence fluctuation spectroscopy.
AUTHOR: Chen Y.; Wei L.-N.; Muller J.D.
CORPORATE SOURCE: L.-N. Wei, Department of Pharmacology, University of Minnesota, 6-120 Jackson Hall, 321 Church Street Southeast, Minneapolis, MN 55455, United States. weixx009@tc.umn.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (23 Dec 2003) 100/26 (15492-15497).
Refs: 27
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . two compared with EGFP alone, demonstrating the sensitivity of molecular brightness as a probe for protein complex formation. Oligomerization of **nuclear receptors** plays a crucial role in the regulation of gene expression. We probe the oligomerization state of the testicular **receptor** 4 and the ligand-binding domains of retinoid X **receptor** and retinoic acid

receptor by observing molecular brightness changes as a function of protein concentration. The large concentration range accessible by experiment allows us to perform titration experiments on EGFP **fusion** proteins. An increase in the molecular brightness with protein concentration indicates the formation of homocomplexes. We observe the formation of **homodimers** of retinoid X **receptor** ligand binding domain upon addition of ligand. Resolving protein interactions in a cell is an important step in understanding cellular. . .

L6 ANSWER 2 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003093056 EMBASE
TITLE: Essential role for the dimerization domain of NuMA-RARα in its oncogenic activities and localization to NuMA sites within the nucleus.
AUTHOR: Dong S.; Qiu J.; Stenoien D.L.; Brinkley W.R.; Mancini M.A.; Tweardy D.J.
CORPORATE SOURCE: D.J. Tweardy, Section of Infectious Disease, Department of Medicine, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, United States. dtweardy@bcm.tmc.edu
SOURCE: Oncogene, (13 Feb 2003) 22/6 (858-868).
Refs: 21
ISSN: 0950-9232 CODEN: ONCNES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Nuclear** mitotic apparatus protein-retinoic acid **receptor** α (NuMA-RARα) is the fourth of five **fusion** proteins identified in acute promyelocytic leukemia (APL) patients. The molecular basis for its oncogenic activity has not been delineated. In gel-shift assays, NuMA-RARα bound to retinoic acid response elements (RAREs) both as a **homodimer** and as a heterodimer with RXRα. The binding profile of NuMA-RARα to a panel of RAREs was very similar to. . . 10(-8)M ATRA. Studies comparing NuMA-RARα with NuMA-RARα(ΔCC) demonstrated that the dimerization or α-helical coiled-coil domain of NuMA was required for **homodimer** formation, transcriptional repression of wild-type RARα, transcriptional activation of STAT3, and stability of the NuMA-RARα/SMRT complex. Confocal fluorescent microscopy of. . . These results indicate that the dimerization domain of NuMA-RARα is critical for each of the known oncogenic activities of NuMA **fusion** proteins as well as its sequestration to **nuclear** sites normally occupied by NuMA and is distinct from RARα.

L6 ANSWER 3 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004003797 EMBASE
TITLE: Functional specificity of two hormone response elements present on the human apoA-II promoter that bind retinoid X receptor α/thyroid receptor β heterodimers for retinoids and thyroids: Synergistic interactions between thyroid receptor β and upstream stimulatory factor 2a.
AUTHOR: Hatzivassiliou E.; Koukos G.; Ribeiro A.; Zannis V.; Kardassis D.
CORPORATE SOURCE: D. Kardassis, Department of Basic Sciences, University of Crete Medical School, Inst. of Molec. Biol. and Biotech., Herakleion GR-71110, Greece. kardasis@imbb.forth.gr
SOURCE: Biochemical Journal, (1 Dec 2003) 376/2 (423-431).
Refs: 40
ISSN: 0264-6021 CODEN: BIJOAK

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . region of the apoA-II (apolipoprotein A-II) promoter contains a thyroid HRE (hormone response element), which strongly binds RXRα (retinoid X **receptor** α)/T(3)Rβ (thyroid **receptor** β) heterodimers and weakly T(3)Rβ **homodimers**, but does not bind other homo- or heterodimers of RXRα or orphan **nuclear receptors**. Transactivation was abolished by point mutations in the thyroid HRE. In co-transfection experiments of HEK-293 (human embryonic kidney 293) cells,. . . 2a) synergistically transactivated the -911/+29 apoA-II promoter in the presence of T(3). USF2a also enhanced the activity of a GAL4-T(3)Rβ **fusion** protein in the presence of T(3) and suppressed the activity of a GAL4-RXRα **fusion** protein in the presence of RA. These findings suggest a functional specificity of the two HREs of the apoA-II promoter. . .

L6 ANSWER 4 OF 16 MEDLINE on STN
ACCESSION NUMBER: 2003199690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12719467
TITLE: Active repression by unliganded retinoid receptors in development: less is sometimes more.
AUTHOR: Weston Andrea D; Blumberg Bruce; Underhill T Michael
CORPORATE SOURCE: Institute for Systems Biology, 1441 N. 34th St., Seattle, WA 98103, USA.. aweston@systemsbiology.org
SOURCE: Journal of cell biology, (2003 Apr 28) 161 (2) 223-8. Ref: 49
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030430
Last Updated on STN: 20030620
Entered Medline: 20030619
AB . . . APL, acute promyelocytic leukemia; dnRARalpha, dominant-negative version of the RARalpha; E, embryonic age; HDAC, histone deacetylase; LCoR, ligand-dependent corepressor; NCoR, **nuclear receptor** corepressor; RA, retinoic acid; RAR, RA **receptor** ; RARE, RXR **homodimer** bound to bipartite response element; RXR, retinoid X **receptor**; TSA, trichostatin A; CYP26, cytochrome p450, 26; TR, thyroid hormone **receptor**. **receptor** (RAR) **fusion** proteins, blocks myeloid differentiation leading to a rare form of leukemia. Our current understanding of the developmental role of retinoid. . .

L6 ANSWER 5 OF 16 EMBASE
on STN
ACCESSION NUMBER: 2002322926 EMBASE
TITLE: Domains of ERRγ that mediate homodimerization and interaction with factors stimulating DNA binding.
AUTHOR: Hentschke M.; Susens U.; Borgmeyer U.
CORPORATE SOURCE: U. Borgmeyer, ZMNH, Universitatsklinikum Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany. uwe.borgmeyer@zmnh.uni-hamburg.de
SOURCE: European Journal of Biochemistry, (2002) 269/16 (4086-4097).
Refs: 60

ISSN: 0014-2956 CODEN: EJBCAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The estrogen **receptor**-related **receptor** γ (ERRγ/ERR3/NR3B3) is an orphan member of the **nuclear receptor** superfamily closely related to the estrogen **receptors**. To explore the DNA binding characteristics, the protein-DNA interaction was studied in electrophoretic mobility shift assays (EMSAs). In vitro translated ERRγ binds as a **homodimer** to direct repeats (DR) without spacing of the **nuclear receptor** half-site 5'-AGGTCA-3' (DR-0), to extended half-sites, and to the inverted estrogen response element. Using ERRγ deletion constructs, binding was found. . . for DNA-independent dimerization. DNA binding of bacterial expressed ERRγ requires additional factors present in the serum and in cellular extracts. **Fusion** proteins of the germ cell **nuclear** factor (GCNF/NR6A1) with ERRγ showed that the characteristic feature to be stimulated by additional factors can be transferred to a. . .

L6 ANSWER 6 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002179478 EMBASE
TITLE: Interactions of STAT5b-RARα, a novel acute promyelocytic leukemia fusion protein, with retinoic acid receptor and STAT3 signaling pathways.
AUTHOR: Dong S.; Tweardy D.J.
CORPORATE SOURCE: D.J. Tweardy, Section of Infectious Disease, Department of Medicine, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, United States. dtweardy@bcm.tmc.edu
SOURCE: Blood, (15 Apr 2002) 99/8 (2637-2646).
Refs: 65
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Signal transducer and activator of transcription (STAT) 5b-retinoic acid **receptor** (RAR) α is the fifth **fusion** protein identified in acute promyelocytic leukemia (APL). Initially described in a patient with all-trans retinoic acid (ATRA)-unresponsive disease, STAT5b-RARα resulted. . . its unresponsiveness to ATRA, we examined the effect of STAT5b-RARα on the activity of myeloid transcription factors including RARα/retinoid X **receptor** (RXR) α, STAT3, and STAT5 as well as its molecular interactions with the **nuclear receptor** corepressor, SMRT, and **nuclear receptor** coactivator, TRAM-1. STAT5b-RARα bound to retinoic acid response elements (RAREs) both as a **homodimer** and as a heterodimer with RXRα and inhibited wild-type RARα/RXRα transactivation. Although STAT5b-RARα had no effect on ligand-induced STAT5b activation, it enhanced interleukin 6-induced STAT3-dependent reporter activity, an effect shared by other APL **fusion** proteins including promyelocytic leukemia-RARα and promyelocytic leukemia zinc finger (PLZF)-RARα. SMRT was released from STAT5b-RARα/SMRT complexes by ATRA at 10(-6). . . whereas TRAM-1 became associated with STAT5b-RARα at 10(-7) M. The coiled-coil domain of STAT5b was

required for formation of STAT5b-RARα **homodimers**, for the inhibition of RARα/RXRα transcriptional activity, and for stability of the STAT5b-RARα/SMRT complex. Thus, STAT5b-RARα contributes to myeloid maturation arrest by binding to RARE as either a **homodimer** or as a heterodimer with RXRα resulting in the recruitment of SMRT and inhibition of RARα/RXRα transcriptional activity. In addition, STAT5b-RARα and other APL **fusion** proteins may contribute to leukemogenesis by interaction with the STAT3 oncogene pathway. .COPYRGT. 2002 by The American Society of Hematology.

L6 ANSWER 7 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002366392 EMBASE
TITLE: Colocalization and ligand-dependent discrete distribution of the estrogen receptor (ER)α and ERβ.
AUTHOR: Matsuda K.-I.; Ochiai I.; Nishi M.; Kawata M.
CORPORATE SOURCE: K.-I. Matsuda, Dept. of Anatomy and Neurobiology, Kyoto Pref. University of Medicine, Kawaramachi Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan
SOURCE: Molecular Endocrinology, (1 Oct 2002) 16/10 (2215-2230). Refs: 45
ISSN: 0888-8809 CODEN: MOENEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To investigate the relationships between the loci expressing functions of estrogen **receptor** (ER)α and that of ERβ, we analyzed the subnuclear distribution of ERα and ERβ in response to ligand in single living cells using **fusion** proteins labeled with different spectral variants of green fluorescent protein. Upon activation with ligand treatment, fluorescent protein-tagged (FP)-ERβ redistributed from. . . using deletion mutants of ERα suggested that the ligand-dependent redistribution of ERα might occur through a large part of the **receptor** including at least the latter part of activation function (AF)-1, the DNA binding domain, **nuclear** matrix binding domain, and AF-2/ligand binding domain. In addition, a single AF-1 region within ERα **homodimer**, or a single DNA binding domain as well as AF-1 region within the ERα/ERβ heterodimer, could be sufficient for the. . .

L6 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001043700 EMBASE
TITLE: [Promyelocytic leukemia, a unique model to design treatments targeting oncogenes].
LA LEUCEMIE AIGUE PROMYELOCYTAIRE : UN PARADIGME DES TRAITEMENTS CIBLES SUR L'ONCOGENE?.
AUTHOR: Lallemand-Breitenbach V.; Zhu J.; De The H.
CORPORATE SOURCE: V. Lallemand-Breitenbach, Cnrs UPR 9051, Universite de Paris VII, Hopital Saint-Louis, 1, avenue Claude-Vellefaux, 75475 Paris Cedex 10, France
SOURCE: Medecine/Sciences, (2001) 17/1 (14-22). Refs: 52
ISSN: 0767-0974 CODEN: MSMSE4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
029 Clinical Biochemistry
LANGUAGE: French

SUMMARY LANGUAGE: English; French

AB All acute promyelocytic leukemia associated translocations involve a **nuclear receptor** gene, RARα. The most common translocation yields a PML/RARα **fusion** protein. PML/RARα **homodimers** with an increased affinity for corepressor proteins account for the block in myeloid differentiation. Interference of the **fusion** protein with PML function is likely responsible for proliferation of the leukemic cells, but the pathways involved are ill understood.. . . induce clinical remissions in patients. How exactly these drugs induce remissions is disputed, but both induce degradation of the PML/RARα **fusion**, retinoic acid targeting its RARα moiety and arsenic its PML moiety. Transgenic mice have demonstrated that the reciprocal RARα/PML **fusion** accelerates and facilitates leukemogenesis. These animals constitute invaluable preclinical models to assess a variety of drugs targeted at the PML/RARα **fusion** or acting downstream on its molecular targets.

L6 ANSWER 9 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000441409 EMBASE

TITLE: Acquisition of oncogenic potential by RAR chimeras in acute promyelocytic leukemia through formation of homodimers.

AUTHOR: Lin R.J.; Evans R.M.

CORPORATE SOURCE: R.M. Evans, Howard Hughes Medical Institute, Salk Inst. for Biological Studies, 10010 North Torrey Pines Road, La Jolla, CA 92037, United States. evans@salk.edu

SOURCE: Molecular Cell, (2000) 5/5 (821-830).
Refs: 52
ISSN: 1097-2765 CODEN: MOCEFL

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
022 Human Genetics
016 Cancer
005 General Pathology and Pathological Anatomy

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The t(15;17) chromosomal translocation in acute promyelocytic leukemia (APL) generates the PML-RARα **fusion** protein. The recruitment of **nuclear receptor** corepressor SMRT/N-CoR and subsequent repression of retinoid target genes is critical for the oncogenic function of PML-RARα. Here we show that the ability of PML-RARα to form **homodimers** is both necessary and sufficient for its increased binding efficiency to corepressor and inhibitory effects on hormonal responses in myeloid differentiation. We further provide evidence that altered stoichiometric interaction of SMRT with PML-RARα **homodimers** may underlie these processes. Finally, we demonstrate that a RXR AF2 mutant recapitulates many biochemical and functional properties of PML-RARα.. . .

L6 ANSWER 10 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999414050 EMBASE

TITLE: Formation of PML/RARα high molecular weight nuclear complexes through the PML coiled-coil region is essential for the PML/RARα-mediated retinoic acid response.

AUTHOR: Grignani F.; Gelmetti V.; Fanelli M.; Rogaia D.; De Matteis S.; Ferrara F.F.; Bonci D.; Grignani F.; Nervi C.; Pelicci P.G.

CORPORATE SOURCE: P.G. Pelicci, European Institute of Oncology, Department of Experimental Oncology, Via Ripamonti, 435-20141 Milan, Italy

SOURCE: Oncogene, (4 Nov 1999) 18/46 (6313-6321).
Refs: 35
ISSN: 0950-9232 CODEN: ONCNES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . RA-sensitivity in APL is mediated by its oncogenic protein, which results from the recombination of the PML and the RA **receptor** α (RARα) genes (PML/RARα **fusion** protein). Ectopic expression of PML/RARα into haemopoietic cell lines results in increased response to RA-induced differentiation. By structure-function analysis of PML/RARα-mediated RA-differentiation, we demonstrated that **fusion** of PML and RARα sequences and integrity of the PML dimerization domain and of the RARα DNA binding region are required for the effect of PML/RARα on RA-differentiation. Indeed, direct **fusion** of the PML dimerization domain to the N- or C-terminal extremities of RARα retained full biological activity. All the biologically. . . weight complexes in vivo. Functional analysis of mutations within the PML dimerization domain revealed that the capacity to form PML/RARα **homodimers**, but not PML/RARα-PML heterodimers, correlated with the RA-response. These results suggest that targeting of RARα sequences by the PML dimerization domain and formation of **nuclear** PML/RARα homodimeric complexes are crucial for the ability of PML/RARα to mediate RA-response.

L6 ANSWER 11 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998227564 EMBASE
TITLE: Interaction of BAG-1 with retinoic acid receptor and its inhibition of retinoic acid-induced apoptosis in cancer cells.
AUTHOR: Liu R.; Takayama S.; Zheng Y.; Froesch B.; Chen G.-Q.; Zhang X.; Reed J.C.; Zhang X.-K.
CORPORATE SOURCE: X.-K. Zhang, Burnham Institute, Cancer Research Center, 10901 N. Torrey Pines Rd., San Diego, CA 92037, United States. xzhang@ljcrf.edu
SOURCE: Journal of Biological Chemistry, (3 Jul 1998) 273/27 (16985-16992).
Refs: 52
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB BAG-1 (also known as HAP46) is an anti-apoptotic protein, which has been shown previously to interact with a number of **nuclear** hormone **receptors**, including **receptors** for glucocorticoid, estrogen, and thyroid hormone. We show here that BAG-1 also interacts with retinoic acid **receptor** (RAR). Gel retardation assays demonstrated that in vitro translated BAG-1 protein could effectively inhibit the binding of RAR but not retinoid X **receptor** (RXR) to a number of retinoic acid (RA) response elements (RAREs). A glutathione S-transferase-BAG-1 **fusion** protein also specifically bound RAR but not RXR. Interaction of BAG-1 and RAR could also be demonstrated by yeast two-hybrid assays. In transient transfection assays, co-transfection of BAG-1 expression plasmid inhibited the transactivation activity of RAR/heterodimers but not RXR/RXR **homodimers**. When stably expressed in breast cancer cell lines, BAG-1 inhibited binding of RAR/RXR

heterodimer to a number of RAREs and. . .

L6 ANSWER 12 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000303761 EMBASE
TITLE: Estrogen receptor, a common interaction partner for a subset of nuclear receptors.
AUTHOR: Lee S.-K.; Choi H.-S.; Song M.-R.; Lee M.-O.; Lee J.W.
CORPORATE SOURCE: Dr. J.W. Lee, College of Pharmacy, Hormone Research Center, Chonnam National University, Kwangju 500-757, Korea, Republic of. jlee@chonnam.chonnam.ac.kr
SOURCE: Molecular Endocrinology, (1998) 12/8 (1184-1192).
Refs: 59
ISSN: 0888-8809 CODEN: MOENEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Nuclear receptors** regulate transcription by binding to specific DNA response elements as **homodimers** or heterodimers. Herein, the yeast and mammalian two-hybrid tests as well as glutathione-S-transferase pull-down assays were exploited to demonstrate that estrogen **receptor** (ER) directly binds to a subset of **nuclear receptors** through protein-protein interactions between ligand-binding domains. These **receptors** include hepatocyte **nuclear** factor 4, thyroid hormone **receptor** (TR), retinoic acid **receptor** (RAR), ERβ, and retinoid X **receptor** (RXR). In yeast cells, a LexA **fusion** protein to the human ER ligand-binding domain (LexA/ER-LBD) was an inert transactivator of a LacZ reporter gene controlled by upstream. . . LexA/ER-LBD differentially modulated the LacZ reporter gene expression when coexpressed with native TRs, RARs, or RXRs. Similarly, cotransfection of these **receptors** in CV1 cells up- or down-regulated transactivations by ER. From these results, we propose that ER is a common interaction partner for a subset of **receptors**, and these interactions should mediate novel signaling pathways in vivo.

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ACCESSION NUMBER: 97126620 EMBASE
DOCUMENT NUMBER: 1997126620
TITLE: Characterization of the response element and DNA binding properties of the nuclear orphan receptor germ cell nuclear factor/retinoid receptor- related testis-associated receptor.
AUTHOR: Zhong Hua Yan; Medvedev A.; Hirose T.; Gotoh H.; Jetten A.M.
CORPORATE SOURCE: Z.H. Yan, Cell Biology Section, Laboratory of Pulmonary Pathobiology, National Institutes of Health, Research Triangle Park, NC 27709, United States. jetten@niehs.nih.gov
SOURCE: Journal of Biological Chemistry, (1997) 272/16 (10565-10572).
Refs: 38
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Recently, we have reported the cloning of the germ cell-specific, **nuclear** orphan **receptor** germ cell **nuclear**

factor (GCNF)/RTR. In this study, we characterize the RTR response elements by an electrophoretic mobility shift assay/polymerase chain reaction-based, DNA. . . with the greatest affinity to response elements containing TCA(AG(G/T)TCA)2 (consensus RTR response element; conRTRE), to which it binds as a **homodimer**. RTR is also able to bind as a monomer to a single core motif TCAAG(G/T)TCA, albeit with a lower affinity.. . . the same stage of spermatogenesis as RTR. The ability of RTR-Ab2 to cause a supershift of an RTR-RTRE complex with **nuclear** extracts from different tissues correlated with the tissue- and development-specific expression of RTR. Transfection of RTR in CV-1 cells was unable to cause RTRE-dependent transactivation of a CAT reporter gene; however, an RTR-VP16 **fusion** protein could induce transactivation through several RTREs, including P2-RE.

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ACCESSION NUMBER: 96130304 EMBASE
DOCUMENT NUMBER: 1996130304
TITLE: Amino-terminal protein-protein interaction motif (POZ-domain) is responsible for activities of the promyelocytic leukemia zinc finger-retinoic acid receptor-α fusion protein.
AUTHOR: Dong S.; Zhu J.; Reid A.; Strutt P.; Guidez F.; Zhong H.-J.; Wang Z.-Y.; Licht J.; Waxman S.; Chomienne C.; Chen Z.; Zelent A.; Chen S.-J.
CORPORATE SOURCE: Shanghai Institute of Hematology, Rui-Jin Hospital, 197 Rui-Jin Road II,Shanghai 200025, China
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1996) 93/8 (3624-3629). ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Promyelocytic leukemia zinc finger-retinoic acid **receptor** α (PLZF- RARα), a **fusion receptor** generated as a result of a variant t(11;17) chromosomal translocation that occurs in a small subset of acute promyelocytic leukemia (APL) patients, has been shown to display a dominant- negative effect against the wild-type RARα/retinoid X **receptor** α (RXRα). We now show that its N-terminal region (called the POZ-domain), which mediates protein-protein interaction as well as specific **nuclear** localization of the wild-type PLZF and chimeric PLZF-RARα proteins, is primarily responsible fur this activity. To further investigate the mechanisms of PLZF- RARα action, we have also studied its ligand-**receptor**, protein-protein, and protein-DNA interaction properties and compared them with those of the promyelocytic leukemia gene (PML)-RARα, which is expressed in. . . and PML-RARα have essentially the same ligand-binding affinities and can bind in vitro to retinoic acid response elements (RAREs) as **homodimers** or heterodimers with RXRα. PLZF-RARα homodimerization and heterodimerization with RXRα were primarily mediated by the POZ-domain and RARα sequence, respectively. Despite having identical RARα sequences, PLZF-RARα and PML-RARα **homodimers** recognized with different affinities distinct RAREs. Furthermore, PLZF-RARα could heterodimerize in vitro with the wild-type PLZF, suggesting that it may play a rule in leukemogenesis by antagonizing actions of not only the retinoid **receptors** but also the wild-type PLZF and possibly other POZ- domain-containing regulators. These different protein-protein interactions and the target gene specificities. . .

L6 ANSWER 15 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 96047974 EMBASE
DOCUMENT NUMBER: 1996047974
TITLE: Characterization of the cyclic adenosine 3',5'-monophosphate response element of the rabbit surfactant protein-A gene: Evidence for transactivators distinct from CREB/ATF family members.
AUTHOR: Michael L.F.; Alcorn J.L.; Gao E.; Mendelson C.R.
CORPORATE SOURCE: Department of Biochemistry, Texas University SW Medical Center, 5323 Harry Hines Boulevard,Dallas, TX 75235-9038, United States
SOURCE: Molecular Endocrinology, (1996) 10/2 (159-170). ISSN: 0888-8809 CODEN: MOENEN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . transcription in fetal lung explants is stimulated by factors that increase intracellular cAMP. In transfected type II cells, expression of **fusion** genes containing 991 bp of 5'-flanking DNA from the rabbit SP-A gene linked to the human GH gene as reporter. . . . CRE(sp-a) (TGACCTCA), differs by one nucleotide from a palindromic CRE (CRE(pal), TGACGTCA), which is known to bind CREB as a **homodimer**. In the present study, we found that mutagenesis of CRE(sp-a) to CRE(pal) also caused a marked decrease in basal and cAMP- induced **fusion** gene expression. The findings of competitive electrophoretic mobility shift assays (EMSA) using fetal rabbit lung **nuclear** extracts suggest that different protein complexes bind CRE(sp-a) and CRE(pal). By UV cross-linking analysis, an .apprx.43-kilodalton protein complex was. . . and CRE(pal); however, purified CREB was ineffective in binding CRE(sp-a) but did bind CRE(pal). In EMSA using fetal rabbit lung **nuclear** proteins, antibodies directed against CREB, CRE modulator (CREM), and activating transcription factor-1 (ATF-1) failed to supershift the complex of proteins. . . a supershift was evident using CRE(pal) as a probe. Moreover, in competition EMSA using radiolabeled CRE(sp-a) and fetal rabbit lung **nuclear** proteins, a purified basic leucine zipper (bLZ) polypeptide failed to compete for binding. By contrast, the bLZ polypeptide competed effectively with CRE(pal) for lung **nuclear** protein binding. This finding suggests that leucine zipper transcription factors do not bind CRE(sp-a). Additionally, expression of a CRE(sp-a):HIS3 **fusion** gene in yeast was unaffected either by CREB or bLZ polypeptides fused to the GAL4 activation domain. By contrast, HIS3 expression was markedly induced both by CREB and bLZ **fusion** proteins in a CRE(pal):HIS3 yeast strain. By competition EMSA using mutagenized CRE(sp-a) oligonucleotides, the critical protein- binding nucleotides in CRE(sp-a) were found to constitute a hexameric element, TGACCT, which corresponds to a binding site for members of the steroid **receptor** superfamily. Since the TGACCT motif is present in the SP-A gene as a single site, we propose that a unique orphan member of the steroid **receptor** superfamily may bind to this element.

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ACCESSION NUMBER: 95255569 EMBASE
DOCUMENT NUMBER: 1995255569
TITLE: The monomer-binding orphan receptor Rev-Erb represses transcription as a dimer on a novel direct repeat.
AUTHOR: Harding H.P.; Lazar M.A.
CORPORATE SOURCE: Univ. of Pennsylvania School of Med., Department of Medicine, 415 Curie Blvd.,Philadelphia, PA 19104-6149, United States

SOURCE: Molecular and Cellular Biology, (1995) 15/9 (4791-4802).
ISSN: 0270-7306 CODEN: MCEBD4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Rev-Erb is an orphan **nuclear receptor** which binds as a monomer to the thyroid/retinoic acid **receptor** half-site AGGTCA flanked 5' by an A/T-rich sequence, referred to here as a Rev monomer site. **Fusion** of Rev-Erb to the DNA binding domain of yeast GAL4 strongly repressed basal transcription of a GAL4-luciferase reporter gene as. . . monomer sites arranged as direct repeats with the AGGTCA motifs separated by 2 bp (Rev-DR2). Remarkably, Rev-Erb bound as a **homodimer** to Rev-DR2 but not to other direct repeats or to a standard DR2 sequence. The DNA binding domain contained all of the determinants for Rev-DR2-specific homodimerization. Rev-Erb bound cooperatively as a **homodimer** to Rev-DR2, and this interaction was 5 to 10 times more stable than Rev-Erb monomer binding to the Rev monomer. . . this repression, consistent with the GAL4 results. However, the Rev-DR2 specificity did not require the C terminus in vivo, since **fusion** of C-terminally truncated Rev-Erb to a heterologous transactivation domain created a transcriptional activator specific for Rev-DR2. In addition to idealized. . . retinoic acid-induced transcription from a naturally occurring Rev-DR2 in the CRBPI gene. Thus, although Rev-Erb is distinguished from other thyroid/steroid **receptor** superfamily members by its ability to bind DNA as a monomer, it functions as a **homodimer** to repress transcription of genes containing a novel DR2 element.

=> s nuclear (s) receptor (s) homofusion
L7 0 NUCLEAR (S) RECEPTOR (S) HOMOFUSION

=> s receptor (s) homofusion
L8 4 RECEPTOR (S) HOMOFUSION

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 1 DUP REM L8 (3 DUPLICATES REMOVED)

=> d l9 ibib kwic

L9 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001469766 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11514059
TITLE: Fusion estrogen receptor proteins: toward the development of receptor-based agonists and antagonists.
AUTHOR: Muyan M; Yi P; Sathya G; Willmert L J; Driscoll M D; Hilf R; Bambara R A
CORPORATE SOURCE: Department of Biochemistry and Biophysics, University of Rochester Medical Center, Rochester, NY 14642, USA.. mesut_muyan@urmc.rochester.edu
CONTRACT NUMBER: HD 24459 (NICHD)
SOURCE: Molecular and cellular endocrinology, (2001 Sep) 182 (2) 249-63.
Journal code: 7500844. ISSN: 0303-7207.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010830
Last Updated on STN: 20020122

Entered Medline: 20011204

AB . . . in the presence of more than one ER species are a heterogenous population of homo- or heterodimers. We engineered a **homofusion** ERalpha as a prototype single-chain **receptor** by genetically conjugating two ER monomers into a covalently fused single-chain protein to obtain a homogeneous population. This permits analysis of symmetrical or asymmetrical mutations that simulate variant homo- and heterodimers. Although a monomer, the **homofusion receptor** exhibited similar biochemical and functional properties to the dimeric ERalpha. We used activation function-2 (AF2) defective mutants as a model. . .

=> s receptor (s) heterofusion
L10 0 RECEPTOR (S) HETEROFUSION

=> s nuclear (s) receptor (s) single (s) chain (s) fusion
L11 10 NUCLEAR (S) RECEPTOR (S) SINGLE (S) CHAIN (S) FUSION

=> dup rem l11
PROCESSING COMPLETED FOR L11
L12 10 DUP REM L11 (0 DUPLICATES REMOVED)

=> d l12 total ibib kwic

L12 ANSWER 1 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004061958 EMBASE
TITLE: Identification of potent human anti-IL-IR(I) antagonist antibodies.
AUTHOR: Fredericks Z.L.; Forte C.; Capuano I.V.; Zhou H.; Vanden Bos T.; Carter P.
CORPORATE SOURCE: Z.L. Fredericks, Department of Antibody Technologies, Amgen Inc., 51 University Street, Seattle, WA 98101-2936, United States. frederiz@amgen.com
SOURCE: Protein Engineering, Design and Selection, (2004) 17/1 (95-106).
Refs: 36
ISSN: 1741-0126 CODEN: PEDSBR
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Interleukin-1 (IL-1) blockade by IL-1 **receptor** antagonist benefits some arthritis patients by reducing joint damage. This fact inspired us to develop antagonist human therapeutic antibodies against IL-1R(I) using phage libraries that display **single-chain** variable fragment (scFv) antibody fragments. Panning libraries against human IL-1R(I) generated 39 unique scFv-phage whose binding to IL-1R(I) was competed. . . producing antibodies in the scFv-Fc format permitted rapid identification of four lead clones (C10, C13, C14, C15) that inhibit NF-κB **nuclear** translocation induced by IL-1. Reformatting these clones as IgG(4) molecules increased their inhibition potency by ≤24-fold. C10 IgG(4) is the. . . cell-surface cynomolgus or murine IL-1R(I), characteristics advantageous for preclinical toxicology and efficacy studies. This study demonstrates the utility of scFv-Fc **fusion** proteins for rapid screening of clones derived from phage libraries to identify antibody leads with therapeutic potential.

L12 ANSWER 2 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003338322 EMBASE

TITLE: ALK(+), CD30(-), CD20(-) large B-cell lymphoma containing anaplastic lymphoma kinase (ALK) fused to clathrin heavy chain gene (CLTC).
AUTHOR: Chikatsu N.; Kojima H.; Suzukawa K.; Shinagawa A.; Nagasawa T.; Ozawa H.; Yamashita Y.; Mori N.
CORPORATE SOURCE: Dr. H. Kojima, Division of Hematology, Institute of Clinical Medicine, University of Tsukuba, Tsukuba, Ibaraki, 305-8575, Japan. hkojima@md.tsukuba.ac.jp
SOURCE: Modern Pathology, (1 Aug 2003) 16/8 (828-832).
Refs: 18
ISSN: 0893-3952 CODEN: MODPEO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . specimens obtained from the ovary showed monomorphic proliferation of large immunoblastic cells with basophilic cytoplasm, round-shaped nuclei with a high **nuclear** to cytoplasmic ratio, and prominent **single** nucleolus. Immunostaining with anti-anaplastic lymphoma kinase (ALK) antibody, ALK1, showed finely granular cytoplasmic staining pattern. These cells were also positive for epithelial membrane antigen, CD4, CD19, CD38, CD138, cytoplasmic IgG, and λ **chain**, but negative for CD30 (Ber-H2), CD56, CD57, and other T- and B-cell markers. Southern blot analyses revealed that Ig heavy and A light **chain** genes, but not T-cell **receptor** (TCR) β gene, were clonally rearranged. Chromosomal analyses by conventional G-banding, spectral karyotyping, and fluorescence in situ hybridization showed complex abnormality involving 2p23, and chromosome 2 was translocated to chromosome 17. As 2;17 translocation resulting in the **fusion** of clathrin heavy **chain** (CLTC) gene with ALK was previously reported in inflammatory myofibroblastic tumor, we performed reverse transcriptase-polymerase **chain** reaction and demonstrated that the lymphoma cells contained CLTC-ALK **fusion** transcript. Under the diagnosis of ALK (+), CD30(-), CD20(-) large B-cell lymphoma, she was treated with conventional combination chemotherapies. However,. . .

L12 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:72267 CAPLUS
DOCUMENT NUMBER: 136:129934
TITLE: Regulating gene expression using single-chain, monomeric gene switchs of fusion proteins comprising ligand binding domains and transcriptional regulating domains
INVENTOR(S): Beerli, Roger; Schopfer, Ulrich; Barbas, Carlos F.
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; The Scripps Research Institute
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002006463	A2	20020124	WO 2001-EP8190	20010716
WO 2002006463	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1303606 A2 20030423 EP 2001-951681 20010716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004504029 T2 20040212 JP 2002-512356 20010716
PRIORITY APPLN. INFO.: US 2000-619063 A 20000718
WO 2001-EP8190 W 20010716

IT Hormone **receptors**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**nuclear**, gene switch comprising; regulating gene expression using **single-chain**, monomeric gene switchs of **fusion** proteins comprising ligand binding domains and transcriptional regulating domains)

L12 ANSWER 4 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002405745 EMBASE
TITLE: Peptide insertion in the DNA-binding domain of fish glucocorticoid receptor is encoded by an additional exon and confers particular functional properties.
AUTHOR: Lethimonier C.; Tujague M.; Kern L.; Ducouret B.
CORPORATE SOURCE: B. Ducouret, Endocrinol. Molec. Reproduction, UMR-CNRS 6026 Bat 13, Universite de Rennes 1, 35042 Rennes Cedex, France. bernadette.ducouret@univ-rennes1.fr
SOURCE: Molecular and Cellular Endocrinology, (30 Aug 2002) 194/1-2 (107-116).
Refs: 42
ISSN: 0303-7207 CODEN: MCEND6
PUBLISHER IDENT.: S 0303-7207(02)00181-8
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The trout glucocorticoid **receptor** (rtGR) contains an additional sequence of nine amino acids located between the two zinc fingers of the DNA-binding domain (DBD) (Endocrinology 136 (1995) 3774). Polymerase **chain** reaction on trout genomic DNA and sequencing were performed in the DBD region, demonstrating that this peptide is encoded by an additional exon of 27 nucleotides between the two exons encoding the two zinc fingers of other **nuclear receptors**. This additional sequence in the rtGR confers a better binding affinity of the **receptor** to a **single** GRE, as shown by gel shift experiments with GST-DBDrtGR **fusion** proteins, deleted or not of the nine amino acids (Δ9). This higher affinity is correlated with a higher constitutive transcriptional activity of the **receptor** on a reporter gene driven by a **single** GRE, but not with the ligand-induced transcriptional activity. Nevertheless, on a double GRE, the wild type and rtGR-Δ9 are equally. . .

L12 ANSWER 5 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002354769 EMBASE
TITLE: Correction of cross-linker sensitivity of Fanconi anemia group F cells by CD33-mediated protein transfer.
AUTHOR: Holmes R.K.; Harutyunyan K.; Shah M.; Joenje H.;

Youssoufian H.

CORPORATE SOURCE: H. Youssoufian, Bristol-Myers Squibb, Clinical Discovery Department, Princeton, NJ 43-4000, United States. hagopy@bcm.tmc.edu

SOURCE: Blood, (15 Dec 2001) 98/13 (3817-3822).
Refs: 27
ISSN: 0006-4971 CODEN: BLOOAW

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Studies have previously described the feasibility of **receptor**-mediated protein transfer in a cell culture model of Fanconi anemia (FA) group C. This study explores the versatility of this approach by using an antibody **single-chain fusion** protein to correct the phenotypic defect in FA group F cells. A 68.5-kd chimeric protein (His-M195FANCF) was expressed, consisting of a His tag, a **single-chain** antibody to the myeloid antigen CD33, and the FANCF protein, as well as a 43-kd His-FANCF **fusion** protein lacking the antibody motif, in Escherichia coli. The nickel-agarose-purified His-M195FANCF protein bound specifically to the surface of HeLa cells transfected with CD33 and internalized through vesicular structures. The **fusion** protein, but not CD33, sorted to the nucleus, consistent with the known **nuclear** localization of FANCF. No similar binding or internalization was observed with His-FANCF. Pretreatment of the transfected cells with chloroquine abolished **nuclear** accumulation, but there was little change with brefeldin A, indicating a minimal if any role for the Golgi apparatus in. . . was noted in CD33-parental cells or CD33(+) FA cells belonging to groups A and C. These results demonstrate that antibody-directed, **receptor**-mediated protein transfer is a versatile method for the delivery of biologically active proteins into hematopoietic cells. .COPYRGT. 2001 by The. . .

L12 ANSWER 6 OF 10 EMBASE
on STN

ACCESSION NUMBER: 2001223769 EMBASE

TITLE: Nuclear transfer protocol affects messenger RNA expression patterns in cloned bovine blastocysts.

AUTHOR: Wrenzycki C.; Wells D.; Herrmann D.; Miller A.; Oliver J.; Tervit R.; Niemann H.

CORPORATE SOURCE: H. Niemann, Department of Biotechnology, Ruakura Research Centre, Hamilton, New Zealand. niemann@tzv.fal.de

SOURCE: Biology of Reproduction, (2001) 65/1 (309-317).
Refs: 77
ISSN: 0006-3363 CODEN: BIREBV

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 001 Anatomy, Anthropology, Embryology and Histology
021 Developmental Biology and Teratology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The successful production of embryos by **nuclear** transfer (NT) employing cultured somatic donor cells depends upon a variety of factors. The objective of the present study was. . . transporter-1, Glut-1; heat shock protein 70.1, Hsp; desmocollin II, Dc II; E-cadherin, E-cad; interferon tau, IF; insulin-like growth factor 2 **receptor**, Igf2r) in **single** blastocysts employing a semiquantitative reverse transcription-polymerase **chain** reaction assay. The results were compared with those for their in vitro (IVP)- and in vivo-generated noncloned counterparts. In experiment 1, employing either

FBA (**fusion** before activation) or AFS (**fusion** and activation simultaneously) to generate NT blastocysts, Hsp mRNAs were not found in NT embryos from either protocol, whereas Hsp. . .

L12 ANSWER 7 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000379386 EMBASE
TITLE: DNA-carrier proteins for targeted gene delivery.
AUTHOR: Uherek C.; Wels W.
CORPORATE SOURCE: W. Wels, Chemotherapeutisches Forschungsinst, Georg-Speyer-Haus, Paul-Ehrlich-Str. 42-44, D-60596 am Main Frankfurt, Germany. wels@em.uni-frankfurt.de
SOURCE: Advanced Drug Delivery Reviews, (15 Nov 2000) 44/2-3 (153-166).
Refs: 74
ISSN: 0169-409X CODEN: ADDREP
PUBLISHER IDENT.: S 0169-409X(00)00092-2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . approaches rely on the activities of natural or recombinant DNA-carrier proteins to achieve uptake and intracellular delivery of plasmid DNA. **Nuclear** proteins such as histones and members of the high mobility group protein family have been shown to condense DNA and. . . cultured cells. Some structural proteins of DNA viruses spontaneously assemble with plasmid DNA and form transfection-competent pseudocapsids. In addition, chimeric **fusion** proteins have been engineered that incorporate in a **single** polypeptide **chain** heterologous protein domains which facilitate binding to plasmid DNA, specific recognition of target cells, induction of **receptor**-mediated endocytosis, and DNA transport through intracellular compartments. Copyright (C) 2000 Elsevier Science B.V.

L12 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:375698 CAPLUS
DOCUMENT NUMBER: 131:28610
TITLE: Single-chain monoclonal antibody fusion reagents that regulate transcription in vivo and methods of screening for such scFv's
INVENTOR(S): Hoeffler, James P.; Russell, Marijane
PATENT ASSIGNEE(S): Invitrogen Corporation, USA
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928502	A1	19990610	WO 1997-US21407	19971128
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9935875	A1	19990616	AU 1999-35875	19971128
EP 1040201	A1	20001004	EP 1997-949553	19971128
R: DE, FR, GB, NL				

PRIORITY APPLN. INFO.: WO 1997-US21407 W 19971128

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**nuclear** hormone, scFv's recognizing; **single-chain** monoclonal antibody **fusion** reagents that regulate transcription in vivo and methods of screening for such scFv's)

L12 ANSWER 9 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998267352 EMBASE
TITLE: Association of p59(fyn) with the T lymphocyte costimulatory receptor CD2: Binding of the Fyn Src homology (SH) 3 domain is regulated by the Fyn SH2 domain.
AUTHOR: Lin H.; Hutchcroft J.E.; Andoniou C.E.; Kamoun M.; Band H.; Bierer B.E.
CORPORATE SOURCE: B.E. Bierer, NHLBI, National Institutes of Health, Bldg. 10, 10 Center Dr., Bethesda, MD 20892, United States. biererb@nih.gov
SOURCE: Journal of Biological Chemistry, (31 Jul 1998) 273/31 (19914-19921).
Refs: 66
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Human CD2 is a 50-55-kDa cell surface **receptor** specifically expressed on the surface of T lymphocytes and NK cells. Stimulation of human peripheral blood T cells with mitogenic. . . sufficient to induce interleukin-2 production and T cell proliferation in the absence of an antigen-specific signal through the T cell **receptor**. CD2 has been shown previously to associate physically with the Src family protein-tyrosine kinases p56(lck) and p59(fyn). We now report. . . with mitogenic pairs of anti-CD2 mAbs enhanced the association of the Fyn polypeptide with the CD2 complex, whereas stimulation with **single** anti-CD2 mAb had minimal effect. Using glutathione S-transferase (GST) **fusion** proteins, we found that CD2 bound to the Src homology (SH) 3 domain of Fyn. Interestingly, the CD2-Fyn association was negatively regulated by the Fyn SH2 domain; CD2 bound poorly to GST **fusion** proteins expressing both the SH2 and SH3 domains of Fyn. However, the inhibitory effect of the Fyn SH2 domain on. . . domain. In addition, we found that the ability of the Fyn SH2 domain to precipitate tyrosine-phosphorylated proteins, including the CD3ζ **chain**, was enhanced after T cell stimulation with mitogenic pairs of CD2 mAbs. Finally, overexpression of a mutated Fyn molecule, in. . . which the ability of the Fyn SH2 domain to bind phosphotyrosine-containing proteins was abrogated, inhibited CD2-induced transcriptional activation of the **nuclear** factor of activated T cells (N-FAT), suggesting a functional involvement of the Fyn SH2 domain in CD2-induced T cell signaling. We thus propose that stimulation through the CD2 **receptor** leads to the tyrosine phosphorylation of intracellular proteins, including CD3ζ itself, which in turn bind to the Fyn-SH2 domain, allowing. . .

L12 ANSWER 10 OF 10 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 97126620 EMBASE
DOCUMENT NUMBER: 1997126620
TITLE: Characterization of the response element and DNA binding properties of the nuclear orphan receptor germ cell nuclear factor/retinoid receptor- related testis-associated

receptor.

AUTHOR: Zhong Hua Yan; Medvedev A.; Hirose T.; Gotoh H.; Jetten A.M.

CORPORATE SOURCE: Z.H. Yan, Cell Biology Section, Laboratory of Pulmonary Pathobiology, National Institutes of Health, Research Triangle Park, NC 27709, United States. jetten@niehs.nih.gov

SOURCE: Journal of Biological Chemistry, (1997) 272/16 (10565-10572).
Refs: 38
ISSN: 0021-9258 CODEN: JBCHA3

COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Recently, we have reported the cloning of the germ cell-specific, **nuclear** orphan **receptor** germ cell **nuclear** factor (GCNF)/RTR. In this study, we characterize the RTR response elements by an electrophoretic mobility shift assay/polymerase **chain** reaction-based, DNA binding site selection strategy. RTR binds with the greatest affinity to response elements containing TCA(AG(G/T)TCA)2 (consensus RTR response. . . element; conRTRE), to which it binds as a homodimer. RTR is also able to bind as a monomer to a **single** core motif TCAAG(G/T)TCA, albeit with a lower affinity. Mutation analysis supports the specific requirements of the 5'-flanking sequence and the. . . the same stage of spermatogenesis as RTR. The ability of RTR-Ab2 to cause a supershift of an RTR-RTRE complex with **nuclear** extracts from different tissues correlated with the tissue- and development-specific expression of RTR. Transfection of RTR in CV-1 cells was unable to cause RTRE-dependent transactivation of a CAT reporter gene; however, an RTR-VP16 **fusion** protein could induce transactivation through several RTREs, including P2-RE.